

Supplementary Material

**Dynamic Angiopoietin-2 Assessment Predicts Mortality and Chronic Course in
Hospitalized Patients with COVID-19**

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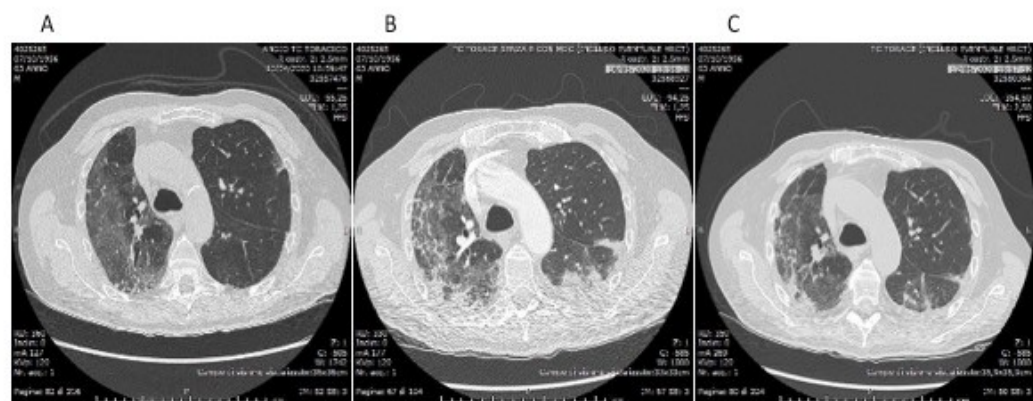
Supplementary Table 1 – Demographic and clinical characteristics of the derivation and validation cohorts

		Derivation cohort	Validation cohort	P
Patients (N)		187	62	
Age (years) (M±SD, median)		69.0±13.4 69.0	67.7±10.8 70.5	0.478
Males (N,%)		135 (72.2)	47 (75.0)	0.572
Intensity of care (n, %)	Medical Ward	71 (38.0)	21 (23.6)	0.843
	Sub-intensive care	70 (37.4)	25 (15.4)	
	Intensive care	46 (24.6)	16 (41.9)	
Deaths (N, %)		53 (28.3)	18 (29.0)	0.663
pO ₂ /FIO ₂ (M±SD, median)		227±95 238	230±102 252	0.961
INR (M±SD, median)		2.4±1 1.26	-	
Bilirubin (mg/dL) (M±SD, median)		1.8±5.6 0.64	-	
CRP (mg/dL) (M±SD, median)		11.2±9.0 9.6	-	
Platelets (×10 ³ /mm ³) (M±SD, median)		207±99 186	195±77 181	0.425
D-Dimer (ug/mL) (M±SD, median)		3.523±5.386 1280	3.940±2.884 3.500	0.216
Hb (g%)		12.8±2.0	-	
HCT		39.6±5.7	38.5±5.4	0.489
WBC (×10 ³ /mm ³)		10.164±10008	-	
Combinated therapy (N, %)	None	4 (2.2)	0	0.0001
	Hydroxychloroquine- Enoxaparine- Tocilizumab	55 (29.6)	4 (6.4)	
	Hydroxychloroquine- Enoxaparine	75 (40.3)	18 (29.0)	
	Hydroxychloroquine- Rezolsta	15 (8.1)	0	
	Hydroxychloroquine alone	28 (15.0)	26 (41.9)	
	Steroids only	10 (5.4)	2 (3.2)	
Ace-inhibitors (N, %)	Yes	26 (15.2)	8 (29.6)	0.064
	No	145 (84.4)	19 (70.3)	
Intervention (N, %)	None	3 (1.6)	2 (3.2)	0.661
	NIV ± pronation	113 (60.4)	38 (61.3)	
	OTI	5 (1.1)	3 (4.8)	
	NIV+ OTI+ pronation	66 (35.9)	19 (30.6)	
Coexisting disorder (N, %)	None	38 (20.8)	13 (20.9)	0.335
	Metabolic disorders, diabetes mellitus, obesity	42 (22.4)	20 (32.2)	

	Cardiovascular disease	27 (14.4)	10 (16.1)	
	Chronic pulmonary disease	17 (9.0)	2 (9.7)	
	Combined	63 (33.6)	17 (27.4)	

NIV: non invasive ventilation; OTI: oro-tracheal intubation

Supplementary Figure 1



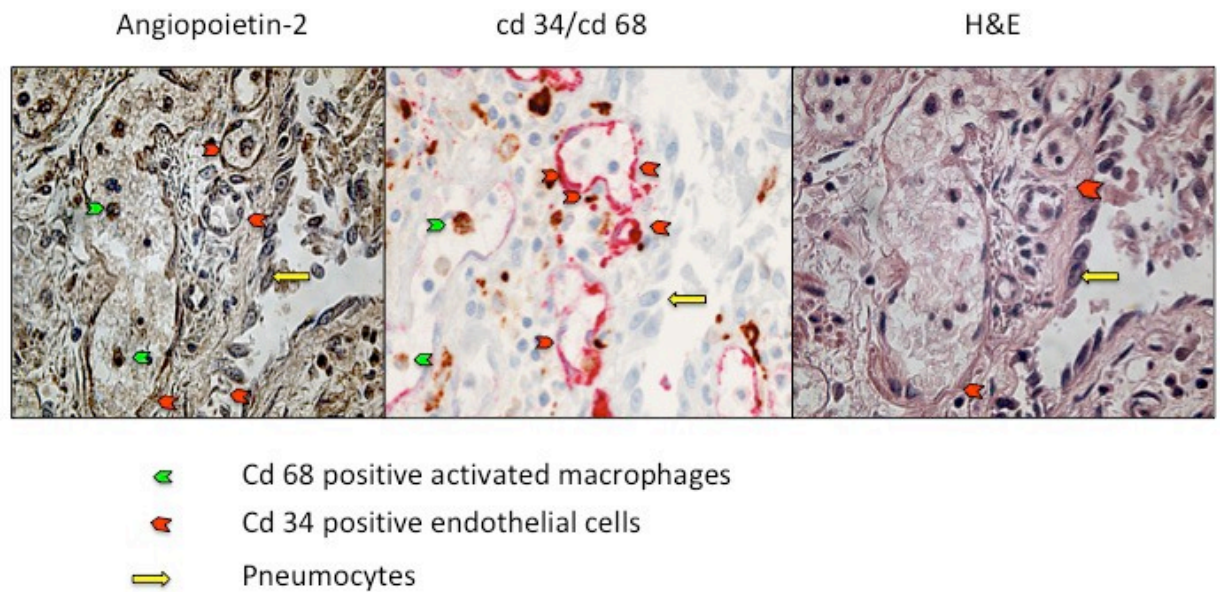
A. CT scan at admission. Extensive right upper lobe ground-glass opacities (GGO) with initial thickening of the interlobular and intralobular septa (crazy paving pattern), especially in the dorsal segment. There is no pleural effusion or air space consolidation at this time.

B. CT scan one month after. Extension of the ground-glass opacity is substantially unchanged, but there is progressive sub-pleural thickening of the interlobular septa and sub-pleural air space consolidations.

C. CT scan 2 months after admission. partial remission of ground-glass opacities and air space consolidations at the right upper lobe but there is persistence of reticular interstitial thickening and initial fibrous changes. There is mild bilateral pleural effusion.

Angiopoietin-2 levels at the time of these scans were 1257 ng/ml (admission), 1339 ng/ml (1 month after) and 1522 ng/ml (2 months after).

Supplementary Figure 2



A proliferative network of capillaries is evident inside the alveolar walls (D: CD34 immunoreactive endothelium in red). The alveolar spaces are filled from macrophages (D: CD68 immunoreactive macrophages in brown). Angiopoietin-2 immunoreactivity colocalizes in mature and newly formed endothelia